08/459,141

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/459,141	06/02/95	BERMAN	P-P0223C6

EXAMINER

18N2/0128

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ART UNIT	PAPER NUMBER
1818	16

DATE MAILED: 01/28/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- [X] Responsive to communication(s) filed on 10/22/97
- [X] This action is **FINAL**.
- [ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- [X] Claim(s) 10-23 is/are pending in the application.
  - Of the above, claim(s) _____ is/are withdrawn from consideration.
- [ ] Claim(s) _____ is/are allowed.
- [X] Claim(s) 10-23 is/are rejected.
- [ ] Claim(s) _____ is/are objected to.
- [ ] Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- [ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
  - [ ] All [ ] Some* [ ] None of the CERTIFIED copies of the priority documents have been
    - [ ] received.
    - [ ] received in Application No. (Series Code/Serial Number) _____.
    - [ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - *Certified copies not received: _____.
- [ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- [ ] Notice of Reference Cited, PTO-892
- [X] Information Disclosure Statement(s), PTO-1449, Paper No(s). 16
- [ ] Interview Summary, PTO-413
- [ ] Notice of Draftperson's Patent Drawing Review, PTO-948
- [ ] Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1818.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The examiner acknowledges receipt of the amendment and exhibit. Since the previous office action was not a final rejection, the response is being viewed as a response to a non-final office action .

4. The examiner acknowledges receipt of the supplemental information disclosure statement. Claims 10-23 are pending and under consideration.

5. Contrary to applicant's statement, the examiner did not indicate that claims 11, 18 and 19 would be allowable if re-written in independent form.

6. It should be note that the provisional double patenting rejection under 35 U.S.C. 101 has been withdrawn (paper no. 11, page 2 of the previous office action).

7. Applicant's arguments filed 10/22/97 have been fully considered but they are not persuasive.

8. The rejection of claims 10-23 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-23 of copending application serial number 08/470,107 and over claims 10-23 of copending application serial number 08/459,147 and the rejection of claims 10, 11, 14-23 under the judicially created doctrine of obviousness-type

double patenting over claims 1, 2, 10, 13, 14, 17, 20-23 of copending application serial number 08/357,084 are maintained for reasons set forth in the previous office actions. The examiner notes, again, applicant's statement concerning the filing of a terminal disclaimer.

9. The rejection of claims 10, 12, 13-17, 20-23 under 35 U.S.C. 112 first paragraph as the disclosure is enabling only for claims limited to a method of producing a glycoprotein D vaccine and a vaccine containing the glycoprotein D of herpes simplex virus is maintained for reasons set forth in the previous office actions.

a) Applicant urges the following: that the facts regarding the prior art and the instant application differ in that the prior art of Watson or Rose suggested problems with the protectiveness of a truncated polypeptide vaccine and the fact that the instant specification enables a truncated glycoprotein D vaccine is indicative of the enablement of mixtures of D, B and C glycoproteins, that the similarity between glycoproteins C and F enables a vaccine mixture of gB, gC and gD truncated glycoproteins, the declarations of Dr. Rose imply the success in using glycoprotein D as a "herpes simplex vaccine model", Dr. Rose refers to the instant invention as providing protection against a pathogen which indicates a scope beyond glycoprotein D, Dr. Secher's reference to a "truncated version of a glycoprotein" supports the full scope of the claimed subject matter, applicant submits exhibit A (Ghiasi et al) in which it is stated that it was published well after the filing date, but enables the full scope of the claimed subject matter and lastly, that the instant application provides enablement for showing protective immunity of

glycoprotein D and coupled with the expression of glycoprotein C one skilled in the art could practice the full scope of the claimed invention.

b) It is the examiner's position that applicant argues similarly as has been argued in previous responses. The specification shows (pages 2-34) cloning and sequencing of the gD genes, expression of the gD glycoprotein, immunization of mice with gD glycoprotein (truncated and full length), and challenge with HSV. The specification also shows (pages 34-47 and example 2) cloning and sequencing of the gC genes, expression of the gC glycoprotein and analysis of the amino acid sequence and the homology and similarity between gC and gF. The specification lacks enablement for a vaccine comprising gC and gD glycoproteins which would protect against HSV-1 and HSV-2 infections and would be more effective than either glycoprotein alone as stated in the specification. Moreover, there is no enablement for a vaccine comprising glycoprotein gB or gA or gE. There is neither guidance nor teaching to show which dosages of the vaccine containing the mixtures would be effective in protection against HSV. The instant specification provides challenge data to show the effectiveness of the gD glycoprotein against HSV-1 and HSV-2 infection. The specification provides no enablement to show that the gC glycoprotein was administered to animal models and challenged with HSV to show the effectiveness of the gC glycoprotein. Additionally, the specification lacks enablement for a mixture of glycoproteins such as gB and gD or gB and gC or any other combination of proteins formulated into a vaccine and injected into animals. Applicant has not pointed to where in the specification there is enablement for a mixture of glycoproteins where the mixture contains, for

example, gB and gD glycoproteins or any other glycoproteins. The recitation that it is believed that other combinations could be used does not provide enablement for a mixture as claimed, but merely an invitation to experiment.

c) It appears that the declarations have argued that it is not only necessary to show that a glycoprotein can be prepared or that a glycoprotein can raise neutralizing antibodies but that it must be protective (see Declaration of Dr. Rose). This protection was not shown for glycoprotein C or B or any combination of glycoproteins. Indeed the declarations support the production of a single truncated glycoprotein D and a vaccine containing the glycoprotein D. There is no description or enablement in any declaration for a glycoprotein B or C or a mixture of glycoproteins. It should be noted that in the EPO discussion Document, page 7, it was stated that while two references disclose natural secretion of gD and gC fragments in culture medium, the immunogenicity activity was not tested. In the instant specification, while the gC glycoprotein was mentioned and expressed in a recombinant system, its immunogenicity was also not tested. Moreover, the declarations of Dr. Rose and Dr. Secher are in response to an opposition by Chiron Corporation concerning the EPO discussion document in which the subject matter is glycoprotein D of HSV. The declarations do not set forth factual data concerning either glycoprotein D or any mixture of glycoproteins. It would appear that the declarations are inviting one to experiment to test whether or not other glycoproteins would be effective in vaccine preparations.

d) Additionally, it appears that Ghiasi et al (exhibit A) are concerned with comparative protection of mice against HSV challenge using glycoproteins B, C, D, E, G, H and I. It is stated

that most immunological vaccine studies of HSV-1 glycoproteins have focussed on gB and/or gD and cites two references, one of Berman et al and the other Glorioso et al. It appears that the Berman article is concerned with glycoprotein D of HSV and the other article is concerned with gC and gB. Ghiasi et al expressed the HSV glycoproteins in a baculovirus system, contrary to how the gD glycoprotein of the instant invention was expressed. Ghiasi et al are quick to point out that different investigators have concluded that different mechanisms are the most important immune responses for protection and recovery, different results have been obtained depending on the vaccine, challenge virus, MHC, mouse strain and route of immunization used and that interpretation of their results should be qualified by the understanding that while valid for their particular experimental system, confirmation in other experimental systems awaits additional studies (page 3123, first column). Thus it appears that one cannot correlate and extrapolate the results of Ghiasi et al, where expression of the glycoproteins was in a baculovirus system back to the result of the glycoprotein D of the instant invention, being expressed in a mammalian system. Additionally, since the gB and gC glycoproteins as claimed in the instant invention, also were not produced and/or tested in the instant invention, particularly similar to Ghiasi et al, one cannot readily extrapolate from Ghiasi et al back to the instant invention concerning mixtures of glycoproteins.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Lynette F. Smith whose telephone number is (703) 308-3909.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald E. Adams, can be reached on (703) 308-0570.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SMITH/lfs
January 26, 1998

L. F. Smith
LYNETTE F. SMITH
PRIMARY EXAMINER
GROUP 1800